

### **DETAILED ACTION**

A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/21/10 has been entered. Claims 3, 8-29, 32-37, 40, 46, and 48-111 have been previously canceled. Claims 1-2, 4-7, 30-31, 38-39, 41-45, 47, and 112-118 are pending and currently under examination. An action on the merits follows.

Those sections of Title 35, US code, not included in this action can be found in a previous office action.

It is again noted that claims 1-2, 4-7, 30-31, 38-39, 41-45, 47, and 112-118 continue to read broadly on any non-human transgenic animal. The claims have been and continue to be examined in view of the elected subject matter, i.e. a transgenic mouse. It is further noted that the species of mouse was elected **without** traverse, and that neither the elected species nor the generic claims are found to be allowable.

### **Claim Rejections - 35 USC § 103**

The rejection of claims 1-2, 4-7, 30-31, 38-39, 41-47, 112-113, and 116-118 under 35 U.S.C. 103(a) as being unpatentable over U.S. 5,859,312 (1/12/99), hereafter referred to as

Littman et al. in view of Mombaerts et al. (1993) Cell, Vol. 75, 275-282, McMurry et al. (1997) Mol. Cell. Biol., Vol. 17 (8), 4553-4561, Rowen et al. (1996) Science, Vol. 272, 1755-1762, and Rack et al. (1997) Blood, Vol. 90(3), 1233-1240, is maintained. Applicant's amendment and arguments have been fully considered but have not been found persuasive in overcoming the rejection for reasons of record as discussed in detail below.

The applicant argues that the claims have been amended to recite that the non-human transgenic animal is capable of producing heterologous T-cell receptors "with a substantial T-cell receptor repertoire", and that this language was suggested by the examiner in the June 29, 2010 interview as a means to overcome the rejection of record.

In response, it is first noted that independent claim 113 has not been amended, and does not recite the added functional language discussed by applicant. Second, as the interview summary of the June 29, 2010 interview mailed to the applicants on 6/30/10 indicated, the idea of including additional functional language in the claims regarding the repertoire of human TCRs present in the transgenic mouse was discussed. However, no specific language was agreed upon. The "functional language" discussion between the examiner and applicant's representatives revolved around applicant's previous arguments that the transgenic mouse according to the instant claims was capable of "normal" T cell development resulting in the generation of a "normal" human T cell TCR repertoire, and that none of the cited references provided a reasonable expectation that mouse T cells having a human TCR repertoire closely resembling the normal human TCR repertoire in a human could be recapitulated in a transgenic mouse comprising human TCR alpha and beta loci. The instant amendment does not reflect this discussion. A "substantial T-cell receptor repertoire" does not place any limitation on the type of

repertoire produced as compared to the normal TCR repertoire in a human, and further does not place an specific limitation on the breadth of the repertoire produced, as the word "substantial" is a relative term which has no specific upper and lower limits. As such, applicant's amendments to the claims have not been found persuasive in overcoming the rejection for reasons of record.

The rejection of claims 114-115 under 35 U.S.C. 103(a) as being unpatentable over U.S. 5,859,312 (1/12/99), hereafter referred to as Littman et al. in view of Mombaerts et al. (1993) Cell, Vol. 75, 275-282, McMurry et al. (1997) Mol. Cell. Biol., Vol. 17 (8), 4553-4561, Rowen et al. (1996) Science, Vol. 272, 1755-1762, and Rack et al. (1997) Blood, Vol. 90(3), 1233-1240 as applied to claims 1-2, 4-7, 30-31, 38-39, 41-47, 112-113, and 116-118 above, and further in view of the NCBI database is maintained. Applicant's amendment and arguments have been fully considered but have not been found persuasive in overcoming the rejection for reasons of record as discussed below.

The applicant argues that the claims have been amended to recite that the non-human transgenic animal is capable of producing heterologous T-cell receptors "with a substantial T-cell receptor repertoire", and that this language was suggested by the examiner in the June 29, 2010 interview as a means to overcome the rejection of record.

In response, as the interview summary of the June 29, 2010 interview mailed to the applicants on 6/30/10 indicated, the idea of including additional functional language in the claims regarding the repertoire of human TCRs present in the transgenic mouse was discussed. However, no specific language was agreed upon. The "functional language" discussion between the examiner and applicant's representatives revolved around applicant's previous arguments that

the transgenic mouse according to the instant claims was capable of "normal" T cell development resulting in the generation of a "normal" human T cell TCR repertoire, and that none of the cited references provided a reasonable expectation that mouse T cells having a human TCR repertoire closely resembling the normal human TCR repertoire in a human could be recapitulated in a transgenic mouse comprising human TCR alpha and beta loci. The instant amendment does not reflect this discussion. A "substantial T-cell receptor repertoire" does not place any limitation on the type of repertoire produced as compared to the normal TCR repertoire in a human, and further does not place any specific limitation on the breadth of the repertoire produced, as the word "substantial" is a relative term which has no specific upper and lower limits. As such, applicant's amendments to the claims have not been found persuasive in overcoming the rejection for reasons of record.

Applicant's amendment has necessitated the following new grounds of rejection.

### **Claim Rejections - 35 USC § 112**

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-2, 4-7, 30-31, 38-39, 41-45, 47, 112, and 114-118 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The applicant has amended independent claims 1, 38, 41, and 112 to recite the limitation that the non-human transgenic animal is capable of producing heterologous T-cell receptors "with a substantial T-cell receptor repertoire". However, the term "substantial" is a relative term with no specific upper and lower limits such that the breadth of the T-cell receptor repertoire encompassed by the claims cannot be determined. Since the metes and bounds of the claims cannot be determined, the claims are indefinite. Note that claims 2, 4-7, 30-31, 39, 42-45, 47, and 114-118 depend on one or more of independent claims 1, 38, 41, and 112 and are therefore included in this rejection.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, the technology center fax number is (571) 273-8300. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197.

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Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

*/Anne Marie S. Wehbé/*

Primary Examiner, A.U. 1633